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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,391	02/20/2004	Pedro Aza-Blanc	P1111US10	6423

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GENOMICS INSTITUTE OF THE
NOVARTIS RESEARCH FOUNDATION
10675 JOHN JAY HOPKINS DRIVE, SUITE E225
SAN DIEGO, CA 92121-1127

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

NOTIFICATION DATE	DELIVERY MODE
10/18/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPLegal@gnf.org
jclarke@gnf.org

Office Action Summary	Application No.	Applicant(s)	
	10/783,391	AZA-BLANC ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2007 and 02 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/13/07 (Request for RCE) and 8/2/07 (revised claim set) has been entered.

2. Claims 27-33 are all the pending claims for this application.

3. Claims 1-5, 9-12 and 21-26 were cancelled and new claims 27-33 added in the Response of 8/2/07.

Specification

4. The amendment to the specification filed in the Response of 8/2/07 has not been entered. Applicants have not identified what amendments have been made to the paragraph [58, 66, and 84] in order for the Examiner to determine that no new matter has been added. Applicants are invited to file a supplemental amendment to the specification.

Withdrawal of Rejections

Claims- 35 USC § 112- second paragraph

5. The rejection of Claim 1 for the recitation "fragment" is withdrawn and moot in view of the cancelled claim.

Applicants' comments on p. 5 of the Response of 8/2/07 are acknowledged.

6. The rejection of Claim 1 for the recitation "modulate TRAIL-induced apoptosis" is withdrawn and moot in view of the cancelled claim.

Applicants' comments on p. 5 of the Response of 8/2/07 are acknowledged.

7. The rejection of Claims 1, 10, 11 and 21-26 as being incomplete for omitting essential steps is withdrawn and moot in view of the cancelled claims.

Applicants' comments on p. 8 of the Response of 8/2/07 are acknowledged.

8. The rejection of Claims 10 and 11 for the limitation "the polypeptide modulator" is withdrawn and moot in view of the cancelled claims.

Applicants' comments on p. 8 of the Response of 8/2/07 are acknowledged.

9. The rejection of Claim 26 as being indefinite for its further limiting to Claim 1 is withdrawn and moot in view of the cancelled claims.

Applicants' comments on p. 8 of the Response of 8/2/07 are acknowledged.

35 USC § 112- first paragraph

Enablement

10. The rejection of Claims 1 and 10-12 under 35 U.S.C. 112, first paragraph, in lacking enablement for a method that identifies a test agent that is specific for both JIK and TRAIL is withdrawn and moot in view of the cancelled claims.

Applicants' comments on pp.6-8 of the Response of 8/2/07 and the Lichtenstein reference are gratuitous in view of the cancelled claims and acknowledged.

11. The rejection of Claim 26 under 35 U.S.C. 112, first paragraph, in lacking enablement for taking a test agent that has been selected through combined method steps a) and b) and further administering the agent to a cancer subject in order to treat the subject is withdrawn and moot in view of the cancelled claim.

Applicants' comments on p. 8 of the Response of 8/2/07 are acknowledged.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 27-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ~~while being enabling for~~ a) screening a test agent in a bioassay measuring JIK kinase activity and in a bioassay measuring TRAIL-induced

apoptosis using an RNAi-based loss of function screening method for identification of test agents/modulators of TRAIL-induced apoptosis in HeLa cells and b) identifying the JIK gene vis-à-vis the RNAi screening method with a JIK-specific RNAi test agent in HeLa cells, does not reasonably provide enablement for identifying any test agent used in the screening method based on modulation of JIK kinase activity and modulation of TRAIL-induced apoptosis vis-à-vis the measurement of any apoptosis activity in any cell or cell line under just any conditions much less in the absence of specific controls, or in using the method in a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability of the art, the breadth of the claims, the quantity of experimentation which would be required in order to use the invention as claimed.

Nature of the Invention/ Skill in the Art

The claims are interpreted as being broadly drawn to screening for agents that modulate TRAIL-induced apoptosis comprising a four step method involving a) screening the biological activity of the JIK protein (kinase activity) in the presence of the agent, step b) identifying an agent from step a), step c) contacting the agent of step b)

with TRAIL in a cell system where JIK is endogenously expressed, and step d) assaying apoptosis activity in the cell system that modulates TRAIL in order to identify an agent that modulates TRAIL-induced apoptosis (Claim 27) where the agent enhances TRAIL-induced apoptosis (Claim 28) or inhibits TRAIL-induced apoptosis (Claim 29), where the cell systems comprises tumor cells (Claim 30) and the tumor cell is a HeLa cell (Claim 31), where the cell system is in a subject (Claim 32) and where step d) comprises assaying caspase activity (Claim 33).

The assay for apoptosis activity in step d) is not limited to an activity exclusively associated with TRAIL, the apoptosis activity may be mediated by any other molecule in a signaling pathway for apoptosis in the cell system. The claims are not limited to any controls, which would distinguish TRAIL-dependent from the TRAIL-independent apoptosis activity. The claims are not limited to the TRAIL-dependent caspase activation being quantitatively different than TRAIL-independent caspase activity.

The relative skill in the art required to practice the invention would be that of a scientist or clinical scientist involved in drug discovery for mechanisms of inhibiting apoptosis.

Disclosure in the Specification

Examples 1 and 2 of the specification and Aza-Blanc et al. (Molecular Cell 12:627-637 (2003); post-filing date publication by the instant inventors) teach a very specific method for identifying genes that effect (enhance/inhibit) TRAIL-induced apoptosis by screening HeLa cells using a siRNA directed against 510 genes including most kinases, i.e., JIK. To identify agents, the effects of the siRNA transfection on cell

viability in the presence and absence of TRAIL was compared. For example, JIK-specific siRNA and *relevant controls* were transfected into HeLa cells in duplicate, and TRAIL was added to one cell group for an additional 24 hr period followed by cell viability measurement. The effect of siRNA on TRAIL-dependent death was calculated as the ratio of viability in the presence versus the absence of TRAIL. Transfection of JIK-specific siRNA into HeLa cells enhanced cell death in a TRAIL-dependent manner. Also, HeLa cells treated with JIK-specific siRNA showed TRAIL-dependent and –independent caspase activity, indicating that JIK has a more general anti-apoptotic role and that removing the biological activity (deleting the gene product) sensitizes cells to TRAIL-induced death.

Additionally, Applicant's specification and Aza-Blanc et al. (p. 631, Col. 1, ¶3) both caution that "one potential concern in using siRNAs for phenotypic screens is that since siRNAs are not 100% selective for the intended mRNA target the observed phenotype could be due to inhibition of either the intended target or an off-target mRNA." It is apparent that in practicing the claimed method invention, one of skill in the art would need to be apprised of the non-specificity for some iRNAs in the targeting method and that performing numerous specific controls would be required to practice the method steps.

The specification does not demonstrate that any other agent than a JIK-specific RNAi was identified by the instant claimed method. The specification is not enabling for a method that would allow one of ordinary skill in the art to identify any test agent that

meets all the limitations of the instant claims much less which could be practiced in a subject.

Thus, without there being a reasonable number of test agents having been identified by the claimed method, the use of the screening method for identifying a specific and substantial test agent is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F,2d 1200, 18 USPQ 1016 (Fed. Cir. 1991) at 18 USPQ 1026 1027 and Ex parte Forman, 230 USPQ 546 (BPAI 1986).

One of skill in the art could not practice the method with a reasonable expectation of success, absent examples providing evidence, which is reasonably predictive for the breadth of the claimed method steps in any cell or cell type, and using just any apoptosis assay in order to correlate the apoptosis activity with TRAIL-induced apoptosis. The enablement provided by the specification is not commensurate in scope with the claimed invention.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER